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ORIGINAL ARTICLE

Associations of CRP, PCT, NC, and NLR with Anti-Infective Effect on Patients with Hematological Malignancy and Pulmonary Infection

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SUMMARY

Background: **We aimed to analyze the associations of C-reactive protein (CRP), procalcitonin (PCT), neutrophil count (NC), and neutrophil-to-lymphocyte ratio (NLR) with the anti-infective effect on hematological malignancy patients complicated with pulmonary infection during chemotherapy.**
Methods: **One hundred hematological malignancy patients complicated with pulmonary infection during chemotherapy admitted from March 2020 through December 2024 were selected as a study group, while another 100 patients without pulmonary infection in the same period were selected as a control group. Their serum CRP and PCT levels, NC, and NLR were compared. The study group was further divided into an effective group and an ineffective group, and the two groups were compared in regards of serum CRP and PCT levels, NC, and NLR.**
Results: **The serum CRP and PCT levels, NC, and NLR in the study group were higher than those in the control group ($p < 0.05$). The serum CRP and PCT levels, NC, and NLR in the ineffective group were higher than those in the effective group ($p < 0.05$). Serum CRP, PCT, NC, and NLR were risk factors for ineffective anti-infective therapy (odds ratio > 1, $p < 0.05$). The areas under the ROC curves of serum CRP, PCT, NC, and NLR alone and in combination for predicting the anti-infective effect were 0.748, 0.818, 0.840, 0.770, and 0.952, respectively.**
Conclusions: **CRP, PCT, NC, and NLR are high in hematological malignancy patients complicated with pulmonary infection during chemotherapy. Their levels are related to the outcome of anti-infective therapy, and the combination of the four can effectively enhance the predictive value.**
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KEYWORDS

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INTRODUCTION

Hematological tumor is a malignancy occurring in the blood system or hematopoietic tissue. The most common hematological tumor is leukemia, which will seriously affect the immune system and hematopoietic system of the human body and poses a serious threat to patient health. Therefore, prompt chemotherapy is required [1]. Chemotherapy can lead to declines in immune function in patients with hematological malignancy, making patients vulnerable to the attack of bacteria, fungi, and other microorganisms, thus developing pul-

monary infection. If no prompt detection and treatment is available, dyspnea and chest pain, and even sepsis or other organ failure may occur. Anti-infective therapy is often applied to hematological malignancy patients complicated with pulmonary infection during chemotherapy. However, the effect of empirical anti-infective therapy varies from person to person, so the question of how to assess the anti-infective effect has become the key to the guidance of subsequent treatment. Therefore, it is a research hotspot to explore convenient and efficient biomarkers for evaluating the anti-infective effect on hematological malignancy patients complicated with pulmonary infection during chemotherapy.

C-reactive protein (CRP) is an acute phase protein that serves as a non-specific marker of inflammation and tissue damage, and its level will rise sharply in case of infection or tissue damage, which is why it is usually used in clinical differential diagnosis of infection [2]. Procalcitonin (PCT) rapidly increases following pathogen infection, showing high sensitivity and specificity for the diagnosis of infectious diseases [3]. Neutrophils, derived from bone marrow, can cause inflammatory responses at the site of infection, playing an important defensive role against infection [4]. Neutrophil-to-lymphocyte ratio (NLR) is a peripheral blood inflammatory indicator derived from blood routine indicators, which can effectively reflect the severity of infection [5]. As can be seen from the abovementioned studies, CRP, PCT, neutrophil count (NC), and NLR are all highly associated with infection, suggesting that they can serve as biomarkers for evaluating the anti-infective effect on hematological malignancy patients complicated with pulmonary infection during chemotherapy.

Therefore, this study aimed to analyze the serum CRP and PCT levels, NC, and NLR in hematological malignancy patients complicated with pulmonary infection during chemotherapy and assess their associations with the anti-infective effect as well as their predictive values.

MATERIALS AND METHODS

Subjects

Patients were consecutively recruited during the study period, based on the inclusion and exclusion criteria to minimize selection bias. One hundred hematological malignancy patients complicated with pulmonary infection during chemotherapy admitted to this hospital from March 2020 through December 2024 were selected as the study group, including 56 males and 44 females aged 20 - 85 years, with a mean age of (60.73 ± 13.92) years. The body mass index (BMI) was 20 - 24 kg/m^2 and averaged at (22.86 ± 0.58) kg/m^2. Another 100 hematological malignancy patients without pulmonary infection during chemotherapy in the same period were selected as a control group, including 54 males and 46 females aged 31 - 84 years, with a mean age of (59.34 ± 13.11) years. BMI was 20 - 24 kg/m^2, with an average BMI of (22.83 ± 0.55) kg/m^2. The gender, age, and BMI were comparable between the two groups ($p > 0.05$). All patients were diagnosed with hematological malignancies based on the World Health Organization (WHO) classification criteria using comprehensive hematological assessments. The diagnostic evaluations were performed by experienced hematopathologists according to institutional protocols that complied with national and international guidelines in hematology. Besides, all enrolled patients received chemotherapy according to standardized protocols specific to their hematological malignancy subtypes, in accordance with current clinical guidelines and institutional practices.

Patient compliance with chemotherapy was assessed through a combination of methods. Chemotherapy administration records were reviewed to confirm that patients completed the prescribed treatment cycles without unjustified interruptions or early discontinuation. Additionally, compliance was cross-verified through electronic medical records (EMRs), including treatment logs and physician progress notes. Follow-up data from hematologists and nursing staff were also considered to document adherence. Only patients with verified adherence to chemotherapy protocols were classified as having good compliance and were included in the analysis. To ensure consistency in diagnostic and treatment protocols over the nearly five-year data collection period, all enrolled patients were diagnosed and managed according to standardized institutional protocols that aligned with national clinical practice guidelines in hematology and infectious diseases. Diagnostic criteria for pulmonary infection were based on consistent radiological, clinical, and microbiological findings throughout the study period and were regularly reviewed by a multidisciplinary team.

Inclusion and exclusion criteria

Inclusion criteria were as follows: 1) for both groups: patients diagnosed with hematological malignancy by bone marrow aspiration and biopsy, 2) for the study group: patients clinically diagnosed with pulmonary infection (presence of cough, fever, expectoration, poor appetite, fatigue, listlessness, and other symptoms, wheezing rale, fine bubbling rale and coarse breath sounds in both lungs heard in physical examinations, and single or multiple patchy increased-density shadows in both lungs or one lung found by chest X-ray or chest CT), 3) patients who could communicate normally, 4) patients who or whose families were informed of this study and signed the informed consent form, and 5) patients with good chemotherapy compliance.

Exclusion criteria involved: 1) patients with an estimated survival period < six months, 2) those lost to follow-up after chemotherapy, 3) those with severe cardio-cerebrovascular diseases, or liver or kidney dysfunction, 4) those who experienced bronchiectasis, chronic obstructive pulmonary disease, lung cancer, interstitial lung disease, tuberculosis, or other lung diseases before chemotherapy, 5) those with contraindications or allergies to

related drugs, 6) those complicated with autoimmune disease or other malignant tumors, 7) those who recently used immunosuppressant drugs, or 8) those with recent or ongoing infections unrelated to chemotherapy or pulmonary complications under investigation.

Measurement of serum CRP and PCT levels, NC, and NLR

To minimize pre-analytical variability, all venous blood samples (5 mL) were collected under standardized conditions. Specifically, patients in both the control and study groups underwent blood collection in the morning after an overnight fast (≥ 8 hours) on the day of enrollment. For patients in the study group (with pulmonary infection), blood samples were obtained at the time of clinical diagnosis of infection, and before the initiation of antibiotic therapy whenever possible. After collection, blood samples were left to stand at room temperature for 30 minutes and centrifuged at 2,500 r/minute for 10 minutes (radius: 10 cm). Then, the upper-layer serum was harvested into centrifuge tubes. Serum CRP (reference range: 0 - 10 mg/L) and PCT (reference range: 0 - 0.5 ng/mL) were measured by double-antibody sandwich enzyme-linked immunosorbent assay [Pointe Biotechnology (Nanjing) Co., Ltd.]. These kits are CE-marked and validated for clinical diagnostic use. According to the manufacturer's instructions, the intra-assay and inter-assay coefficients of variation (CVs) for both CRP and PCT assays were < 10% and < 15%, respectively. Assay performance was periodically monitored using quality control samples to ensure consistency and reliability throughout the study. NLR (reference range: 0 - 10) and NC (reference range: 1.8 - 6.3 × 10^9/L) were measured using an automatic blood cell analyzer (Beckman Coulter, USA).

Anti-infective therapy protocol

The patients were treated with antibiotics such as carbapenems, cephalosporins, glycopeptides, and glycylcyclines, either alone or in combination. The selection and application of antibiotics were tailored individually based on each patient's clinical presentation, drug susceptibility results, underlying disease status, and organ function, under the guidance of experienced infectious disease specialists according to related guidelines [6,7].

To ensure adherence, antibiotic administration was supervised by attending physicians and recorded in the hospital's electronic medical records system. Medication use was reviewed daily during ward rounds, and any deviations or adverse reactions were promptly addressed. Patient compliance was further monitored through nursing documentation and regular assessments of clinical response and laboratory indicators.

Assessment of clinical efficacy

After anti-infective therapy in the study group, the efficacy was assessed, covering cure (disappearance of cough, purulent sputum, fever, hemoptysis, and other clinical symptoms, disappearance of lung wheezing and moist rales, normal blood routine indicators, and no shadow and effusion in the lungs found in X-ray images), improvement (great improvement in clinical symptoms, reduction of lung wheezing and moist rales, improvement in blood routine indicators, and obvious absorption of shadow and effusion in the lungs found in X-ray images), and ineffective (no change or even aggravation of clinical symptoms, and enlarged shadow in the lungs found in X-ray images). Cure or improvement cases were included in the effective group, while ineffective cases were included in the ineffective group. The assessment of clinical efficacy was performed on Day 7 after the initiation of anti-infective therapy, in line with standard clinical practice for evaluating treatment response in hospital-acquired and chemotherapy-associated pulmonary infections.

To minimize observer bias, clinical efficacy evaluations were conducted by two independent attending physicians who were blinded to the patients' group allocation and treatment history. In cases of disagreement, a third senior clinician was consulted to reach a consensus.

Collection of general data

Gender, age, clinical stage, BMI, albumin level, agranulocytosis (yes or no), white blood cell count, lymphocyte count, monocyte count, eosinophil count, mean corpuscular volume, mean corpuscular hemoglobin concentration, platelet count, hematocrit, and plateletcrit were recorded in the effective and ineffective groups.

Statistical analysis

SPSS 27.0 software was used for statistical analysis. All measurement data were tested for normality. Measurement data with normal distribution were described as mean ± standard deviation ($\bar{x} \pm s$) and compared by the independent-samples *t*-test between two groups and by the paired-sample *t*-test within the group. For the comparisons among three or more groups, one-way analysis of variance followed by Bonferroni post-hoc tests was used. To identify potential risk factors influencing the anti-infective effect in hematological malignancy patients with pulmonary infection during chemotherapy, binary logistic regression analysis was performed. Candidate variables for inclusion in the multivariate model were first screened using univariate analysis ($p < 0.1$). Variables with clinical relevance and statistical significance were entered into the logistic regression model using a stepwise forward likelihood ratio method. To ensure model validity, multicollinearity among the independent variables was assessed by calculating the variance inflation factor (VIF). Variables with VIF > 10 were considered to indicate multicollinearity and were excluded or adjusted accordingly. In addition, sensitivity analyses were conducted to evaluate the robustness of the logistic regression results.

Receiver operating characteristic (ROC) curves were plotted to analyze the efficiency of CRP, PCT, NC, and NLR alone and in combination for predicting the anti-infective effect on hematological malignancy patients

Table 1. Serum CRP and PCT levels, NC, and NLR in study and control groups ($\bar{x} \pm s$).

Group	n	CRP (mg/L)	PCT (ng/mL)	NC (× 10^9/L)	NLR
Study	100	110.96 ± 10.10	2.89 ± 0.23	12.25 ± 1.03	15.56 ± 1.24
Control	100	50.80 ± 5.15	0.75 ± 0.20	6.35 ± 0.52	10.25 ± 0.52
t		53.064	70.211	51.135	39.491
p		< 0.001	< 0.001	< 0.001	< 0.001

Table 2. Relevant indicators in effective and ineffective groups ($\bar{x} \pm s$).

Indicator		Effective group (n = 80)	Ineffective group (n = 20)	Statistical value	p
Gender	male	45 (48.75)	11 (45.00)	0.010	0.920
	female	35 (51.25)	9 (55.00)		
Agranulocytosis	yes	15 (18.75)	5 (25.00)	0.098	0.755
	no	65 (81.25)	15 (75.00)		
Age (years)		60.95 ± 12.84	60.48 ± 13.87	0.144	0.886
Albumin (g/L)		30.63 ± 5.39	30.41 ± 5.52	0.163	0.871
White blood cell count (× 10^9/L)		3.52 ± 0.28	3.56 ± 0.27	0.575	0.566
Lymphocyte count (× 10^9/L)		6.00 ± 0.52	6.03 ± 0.53	0.230	0.819
Monocyte count (× 10^9/L)		0.50 ± 0.03	0.51 ± 0.04	1.243	0.217
Eosinophil count (× 10^9/L)		0.60 ± 0.04	0.59 ± 0.05	0.950	0.345
Platelet count (× 10^9/L)		170.05 ± 10.25	171.07 ± 10.26	0.398	0.692
Mean corpuscular volume (fL)		80.02 ± 9.24	81.05 ± 9.20	0.446	0.656
Mean corpuscular hemoglobin concentration (g/L)		314.21 ± 20.10	313.25 ± 20.18	0.191	0.849
Hematocrit (%)		30.52 ± 5.21	31.58 ± 5.26	0.812	0.419
Plateletcrit (%)		0.20 ± 0.02	0.21 ± 0.03	1.794	0.076
Serum CRP (mg/L)		86.64 ± 8.87	208.24 ± 12.86	49.776	< 0.001
Serum PCT (ng/mL)		2.15 ± 0.18	5.85 ± 0.22	78.548	< 0.001
NC (× 10^9/L)		11.52 ± 1.20	15.17 ± 1.26	12.048	< 0.001
NLR		14.50 ± 1.26	19.80 ± 1.35	16.589	< 0.001

Table 3. Results of logistic regression analysis of anti-infective effect on hematological malignancy patients complicated with pulmonary infection during chemotherapy.

Item	*B*	Standard error	Wals	p	Odds ratio	95% confidence interval
CRP	0.022	0.007	10.816	0.001	1.022	1.009 - 1.036
PCT	0.121	0.056	4.709	0.030	1.129	1.012 - 1.259
NC	0.273	0.128	4.515	0.034	1.314	1.021 - 1.690
NLR	0.200	0.078	6.622	0.010	1.222	1.049 - 1.423
Constant	10.010	2.298	18.965	0.000	-	-

Table 4. Value of serum CRP, PCT, NC, and NLR alone and in combination for predicting the anti-infective effect on hematological malignancy patients complicated with pulmonary infection during chemotherapy.

Item	Optimal cutoff	Area under the curve	Standard error	p	95% confidence interval	Sensitivity	Specificity	Youden index
CRP	11.920 mg/L	0.748	0.078	0.001	0.595 - 0.900	0.900	0.600	0.500
PCT	4.345 ng/mL	0.818	0.045	< 0.001	0.731 - 0.905	0.700	0.900	0.600
NC	13.695 × 10^9/L	0.840	0.063	< 0.001	0.716 - 0.964	0.838	0.850	0.688
NLR	15.915	0.770	0.070	< 0.001	0.632 - 0.908	0.913	0.600	0.513
Combination	-	0.952	0.022	< 0.001	0.909 - 0.994	0.889	0.719	0.608

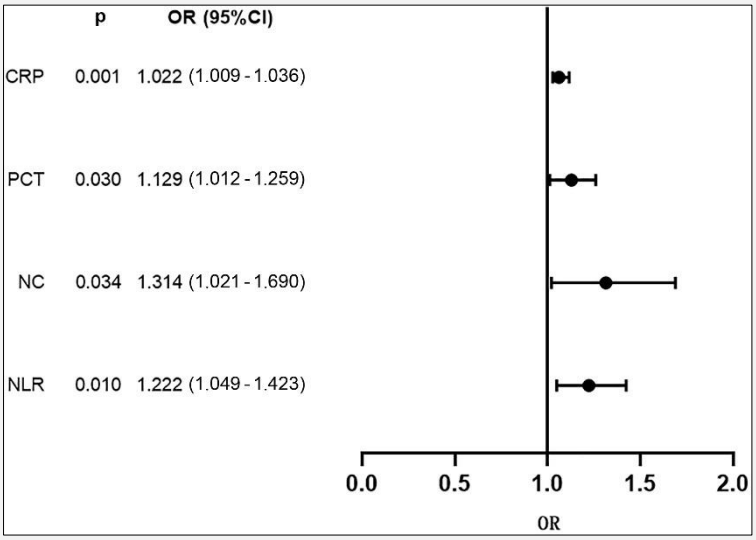

Figure 1. Forest plot of clinical characteristics based on multivariate logistic regression analysis.

complicated with pulmonary infection during chemotherapy. The area under the curve (AUC) > 0.9, = 0.71 - 0.9, = 0.5 - 0.7, and < 0.5 suggested high, certain, low, and no predictive efficiency, respectively. $p < 0.05$ was considered statistically significant.

RESULTS

Serum CRP and PCT levels, NC, and NLR in study and control groups

The serum CRP and PCT levels, NC, and NLR in the study group were higher than those in the control group ($p < 0.05$) (Table 1).

Clinical efficacy

After anti-infective therapy for hematological malignancy patients complicated with pulmonary infection during chemotherapy, 30 cured cases (30.00%), 50 improved cases (50.00%), and 20 ineffective treatment cases (20.00%) were observed. Therefore, there were 80 effective treatment cases (80.00%) and 20 ineffective treatment cases (20.00%).

Relevant indicators in effective and ineffective groups

No statistically significant differences were found in gender, age, albumin, white blood cell count, lymphocyte count, monocyte count, eosinophil count, mean corpuscular volume, mean corpuscular hemoglobin concentration, platelet count, hematocrit, plateletcrit, and

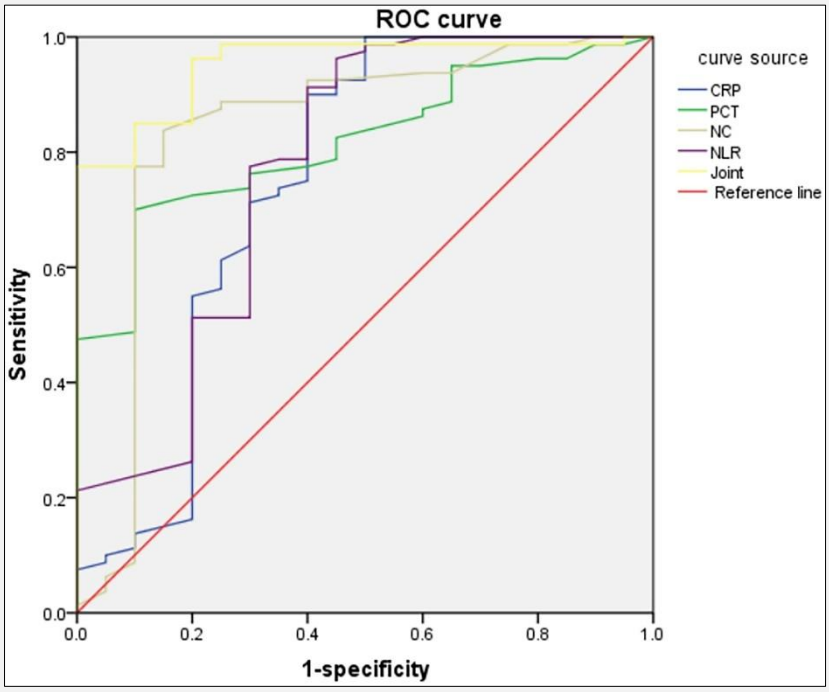

Figure 2. ROC curves for evaluating anti-infective effect on hematological malignancy patients complicated with pulmonary infection during chemotherapy.

agranulocytosis between the effective group and the ineffective group ($p > 0.05$). The serum CRP and PCT levels, NC, and NLR rose in the ineffective group compared with those in the effective group ($p < 0.05$) (Table 2).

Results of logistic regression analysis of anti-infective effect on hematological malignancy patients complicated with pulmonary infection during chemotherapy

Logistic regression analysis revealed that serum CRP, PCT, NC, and NLR were risk factors for ineffective anti-infective therapy in hematological malignancy patients complicated with pulmonary infection during chemotherapy [odds ratio (OR) > 1, $p < 0.05$] (Table 3 and Figure 1).

Value of serum CRP, PCT, NC, and NLR alone and in combination for predicting the anti-infective effect on hematological malignancy patients complicated with pulmonary infection during chemotherapy

ROC curves were drawn, with the anti-infective effect on hematological malignancy patients complicated with pulmonary infection during chemotherapy as state variables (0: ineffective group, 1: effective group), and serum CRP and PCT levels, NC, and NLR as test variables. The AUCs of serum CRP, PCT, NC, and NLR alone and in combination for predicting the anti-infective effect were 0.748 [95% confidence interval (CI): 0.595 - 0.900], 0.818 (95% CI: 0.731 - 0.905), 0.840 (95% CI: 0.716 - 0.964), 0.770 (95% CI: 0.632 - 0.908), and 0.952 (95% CI: 0.909 - 0.994), respectively (Table 4 and Figure 2).

DISCUSSION

The incidence of hematological malignancy has been increasing year by year in recent years due to environmental pollution, lifestyle changes, and other factors. Pulmonary infection is a common clinical complication of hematological malignancy patients undergoing chemotherapy, which will aggravate the condition of these patients. In addition, due to the toxic side effects of chemotherapy drugs, some patients will choose to give up chemotherapy, making the clinical treatment and infection control more difficult and affecting prognosis [8,9]. Therefore, effective anti-infective measures should be taken promptly for hematological malignancy patients complicated with pulmonary infection during chemotherapy.

The effectiveness of anti-infective therapy is a critical determinant for subsequent treatment for infectious diseases [10]. Therefore, identifying reliable biomarkers to precisely evaluate the efficacy of anti-infective therapy is imperative for subsequent management of hematological malignancy patients complicated with pulmonary infection during chemotherapy. CRP, an acute-phase protein synthesized by the liver in response to pathogen invasion or tissue damage, has, under normal circumstances, a minimal level in blood of healthy people, but it can rapidly increase in a short time once synthesized, making it a highly sensitive and non-specific biomarker for reflecting the degree of inflammation, tissue damage, and infection [11,12]. PCT is a protein released by cells upon bacterial infection, and its content in normal people is extremely low and almost undetectable. When the human body is severely infected with bacteria, fungi, and parasites, PCT will be cleaved into calcitonin by proteolytic enzyme in a short time, thus displaying abnormal increases [13]. In this study, the results showed that the levels of serum CRP and PCT in the study group were higher than they were in the control group, and logistic regression analysis revealed that high levels of serum CRP and PCT were risk factors for ineffective anti-infective therapy in hematological malignancy patients complicated with pulmonary infection during chemotherapy. It can be seen that elevations of CRP and PCT can significantly raise the risk of failure of anti-infective therapy in hematological malignancy patients complicated with pulmonary infection during chemotherapy. The main reasons are as follows: First, CRP can activate inflammatory signaling pathways and enhance the infiltration of inflammatory factors to alveolar epithelial tissues, aggravating lung tissue damage and infection, and making anti-infective therapy more difficult. As a result, the risk of ineffective anti-infective therapy significantly increases [14]. Second, the higher the PCT level, the more severe the infection, making anti-infective therapy more difficult and significantly increasing the risk of failure of anti-infective therapy [15].

In this study, elevated NC and NLR were also identified as risk factors for anti-infective effect on hematological malignancy patients complicated with pulmonary infection during chemotherapy, suggesting that measures should be taken to reduce the levels of NC and NLR to lower the risk of pulmonary infection and further improve the efficacy. The reasons are as follows: First, as the first defense barrier against external infection, neutrophils play an important role in the defense and protection of the human body. Neutrophils will respond quickly and migrate to the site of infection to phagocytize and kill pathogens when the body is infected by bacteria or viruses. A higher NC suggests a stronger response of the body to infection, and it also reflects to some extent the more severe pulmonary infection during chemotherapy for hematological malignancy, thus causing sepsis easily and increasing the risk of ineffective anti-infective therapy [16-18]. Second, NLR is defined as the ratio of neutrophils to lymphocytes. Neutrophils can secrete a variety of cytokines to regulate the function of epithelial cells, mast cells, and macrophages, thereby playing a vital role in non-specific inflammatory processes. Lymphocytes, mainly present in lymph, have immune recognition function and play a central role in immunoregulation and immune response [19,20]. The increases in NLR are considered to be related to a relative increase in neutrophils and a significant decrease in lymphocytes, indicating imbalance of inflammatory responses and immune response. A higher NLR corresponds to more serious pulmonary infection, which can greatly increase the risk of ineffective anti-infective therapy [21,22].

The areas under the ROC curves of serum CRP, PCT, NC, and NLR alone and in combination for predicting the anti-infective effect were 0.748, 0.818, 0.840, 0.770, and 0.952, respectively. It can be seen that CRP, PCT, NC, and NLR can serve as efficient biomarkers for predicting the anti-infective effect on hematological malignancy patients complicated with pulmonary infection during chemotherapy, and combined detection of the four can effectively improve their predictive value. The reason for that is that the physiological elevation of a single indicator caused by disease factors, drug use, and diet can be excluded by combined detection, and comprehensive analysis of multiple indicators can compensate for the limitation of any single indicator, thereby more accurately determining the anti-infective effect. Therefore, we should closely monitor the serum CRP and PCT levels, as well as NC and NLR before anti-infective therapy in hematological malignancy patients complicated with pulmonary infection during chemotherapy, stay alert to patients with high levels of the four, and take targeted interventions to ameliorate their prognosis.

The present study also has some limitations. For example, the exclusion of patients with pre-existing pulmonary diseases such as bronchiectasis, chronic obstructive pulmonary disease, lung cancer, interstitial lung disease, and tuberculosis may limit the generalizability of the findings to the broader population of hematological malignancy patients. Future studies should consider including such patients to evaluate the applicability of inflammatory biomarkers across more diverse clinical settings.

In conclusion, CRP, PCT, NC, and NLR are high in hematological malignancy patients complicated with pulmonary infection during chemotherapy. CRP, PCT, NC, and NLR levels are related to the outcome of anti-infective therapy, and the combination of the four can effectively enhance the predictive value for the anti-infective effect.

Ethical Approval and Consent to Participate:

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Bengbu Medical University (approval number: [2025]KY085). All subjects

provided written informed consent prior to participation.

Availability of Data and Materials:
The datasets generated and analyzed during the study are available from the corresponding author on reasonable request.

Declaration of Interest:
The authors declare no conflict of interest.

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